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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,652	08/07/2001	Ronald A. Laskey	620-161	9664

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EXAMINER	
NICKOL, GARY B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding..

Office Action Summary	Application No.	Applicant(s)	
	09/922,652	LASKEY ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88,89,101,102,104,105 and 107-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88,89,101,102,104,105 and 107-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Laskey *et al.*

Date of priority: 05/15/1998

Request for Continued Examination

The request filed on 12-16-2004 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/922652 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 88-89, 101-102, 104-105, 107-111 are pending.

New Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 89 and 108 are rejected under 35 U.S.C. 112, second paragraph, as being vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 89 and 108 appear vague and inconsistent with the required steps set forth in independent claim 88. For example, claim 89 appears to further define a different correlation between the presence of dysplasia/neoplasia simply by the binding of antibody or antibody fragment to the MCM2 protein in the test sample. However, independent claim 88 requires that

the deciding correlation (between antibody and the presence of dysplasia/neoplasia) exist solely as an "increase" in the amount of binding or a "difference" in the pattern of binding. Thus, it's not clear how claims 89 and 108 relate to and/or further limit the subject matter of claim 88. In other words, there does not appear to be an antecedent basis for this type of correlation found in Claims 89 and 108.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 88-89, 101-102, 104-105, 107-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todorov *et al.* (Laboratory Investigation, Vol. 78, No. 1, pp. 73-78, January 1998, *previously cited*) in combination with the teachings of Murphy *et al.* (Clinical Oncology, 2nd Edition, Chapter 5, 1995).

Todorov *et al.* teaches a method of contacting normal human tissues and primary human tumors with an antibody directed against MCM2 whereby an increase in said amount and/or a difference in said pattern compared with normal is indicative of the presence of dysplasia or neoplasia. Specifically, the authors analyzed a variety of human tissues (i.e., breast, colorectal, kidney, lung, etc., See Table 1, page 74) wherein MCM2 was detectable by immunoblotting in 97% of the studied tumors versus only 27% of the corresponding normal samples (see abstract).

Todorov *et al.* does not teach detecting MCM2 by obtaining a test sample containing cells derived from **sputum, bronchio-alveolar lavage specimens, urine, breast duct fluid, brushings from the alimentary tract, and cervical, fecal, or urine cytology smears wherein a population of individuals is screened.**

Murphy *et al.* teach various routine methods commonly used at the time the invention was made for the laboratory diagnosis of cancer including analyzing cells from tissue brushings or fluids, i.e. "cytology" (see page 82, 1st column), electron microscopy, immunohistochemistry of frozen tissues (page 85), in situ hybridization (page 86), and DNA probe analysis (page 88). The reference summarizes (page 94, bottom of 1st column) that this overview has covered a number of "conventional" and recent techniques available to the pathologist for use in the evaluation of neoplastic diseases.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to determine the amount and/or staining patterns of MCM2 in a population of individuals comprising contacting cells derived from sputum, bronchio-alveolar lavage specimens, urine, breast duct fluid, brushings from the alimentary tract, and cervical, fecal, or urine cytology smears with an antibody directed against MCM2 because immunohistochemistry

of tumor tissues and cytological analysis (i.e., the analysis of cells derived from sputum, cervical, fecal, urine specimens, etc.) are well-known and routinely employed techniques for the pathological evaluation of neoplastic disease (see Murphy *et al.* above). Moreover, one of ordinary skill in the art would have a reasonable expectation of success of determining the presence or absence of dysplasia or neoplasia because the prior art established a direct correlation between the amount and/or difference in MCM2 staining with various human cancerous tissues versus their normal counterparts. Additionally, one would have been motivated to include a test "cervical smear" because it was well-established that adenocarcinomas of the cervix account for up to 20% of cervical carcinomas (See Office Action mailed 09-23-2003, page 7). Combining the latter with the fact that the prior art successfully teaches that MCM2 expression is a novel marker for cell proliferation and that differential staining of MCM2 correlates with a *variety* of adenocarcinomas (Todorov, Table 1, page 74) one clearly would have a reasonable expectation of success that detection of MCM2 would determine the presence or absence of cervical neoplasia or dysplasia.

No claim is allowed.

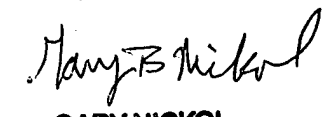
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN



GARY NICKOL
PRIMARY EXAMINER